

## REMARKS

Claims 14 and 20 are pending. Claims 15 and 31 have been canceled without prejudice or disclaimer and solely for the purpose of expediting prosecution. Claims 3-6, 8-9, 12-13, 16-19, 21-22, 24-25, and 27-28 were previously canceled. Claims 1-2, 7, 10-11, 23, 26, and 29-30 are withdrawn. Claims 14 and 20 have been amended to recite that the isolated recombinant megakaryocyte tyrosine kinase 1, or fusion protein thereof, has the amino acid sequence of SEQ ID NO. 2. Support for this amendment is found throughout the specification; see, for instance, the legend for Figure 9 at page 9 of the specification and the third and fourth paragraphs of page 13.

### II. Applicants overcome the Examiner's rejections

1. The Examiner states that "[T]he title of the invention is not descriptive." Office Action at page 2. Applicants have amended the title to reflect that the claimed invention is directed to a "Novel Megakaryocytic Protein Tyrosine ~~Kinases~~ Kinase 1."

2. The Examiner states that "[T]he abstract of the disclosure is objected to because the abstract is in two paragraphs." Office Action at page 2. Accordingly, Applicants have combined the two paragraphs into one and have appended a clean copy of the abstract, on a separate sheet, to this paper.

3. Applicants have amended page 1 of the specification to relate the lineage of the present application, *i.e.*, that it is a divisional application of U.S. application serial no. 08/232,545, filed on April 22, 1994, now U.S. patent No. 6,506,578. Applicants also have submitted an Application Data Sheet conveying this lineage.

4. The Examiner rejected claims 14, 15, 20, and 31 under 35 U.S.C. § 112, second paragraph for (a) reciting "an isolated recombinant MKK1" in claim 14; (b) reciting Figures 1A, 1B, and 1C for the sequence of MKK1 in claim 15; and (c) for reciting "MKK1 protein." Office Action at page 3.

Applicants have amended the claims to recite a "megakaryocyte tyrosine kinase 1" and to specify that the megakaryocyte tyrosine kinase 1 protein has the amino acid sequence

of SEQ ID NO. 2. For these reasons, Applicants respectfully request that the Examiner withdraw these rejections.

5. The Examiner rejected claims 14 and 20 under 35 U.S.C. § 112, first paragraph as lacking written description, because “the specification does not disclose all the MKK1 polypeptides.” Office Action at page 4.

Applicants have amended claims 14 and 20 to recite that a megakaryocyte tyrosine kinase 1 protein has the amino acid sequence of SEQ ID NO. 2, for which there is sufficient written description support. The Examiner acknowledges that “the specification discloses MKK1 polypeptide of SEQ ID NO. 2. This meets the written description and enablement provisions of 35 U.S.C. § 112, first paragraph” (emphasis added; Office Action at page 4). Accordingly, Applicants submit that there is written description for the presently claimed invention and respectfully request that the Examiner withdraw this rejection.

6. The Examiner rejected claims 14 and 20 under 35 U.S.C. § 112, first paragraph as lacking enablement because “the lack of description of the various MKK1 forms in the specification does not enable one of skilled in the art [to] make and/or use the invention.” Office Action at page 6.

Applicants’ amendment overcomes the rejection for the reasons cited in the previous subsection, which also is in keeping with the Examiner’s acknowledgement that an MKK1 of SEQ ID NO. 2 is enabled. See page 7 of the Office Action. Accordingly, Applicants submit that the presently claimed invention is enabled and respectfully requests that the Examiner withdraw this rejection.

7. Claims 14 and 15 are rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Bennett *et al.*, *J. Biol. Chem.*, 269(2), pp. 1068-74, January 14, 1994, or Sakano *et al.*, *Oncogene*, 9(4), pp. 1155-61, April, 1994. Office Action at pages 8 and 9.

Applicants have filed herewith a declaration executed by Ricardo Martinez, a research scientist who was employed at Sugen, which is a collaborator of the assignee of the present application (Max-Planck). Dr. Martinez attests that he sequenced the claimed megakaryocyte

tyrosine kinase 1 before the publication date of Bennett *et al.* Since the declaration antedates both of the cited references, neither is available as prior art against the present claims. Accordingly, none of the claims are anticipated and, thus, this rejection is moot.

8. Claims 20 and 31 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bennett *et al.*, *supra*, or Sakano *et al.*, *supra*, in view of Maniatis *et al.*, 1982, pages 422-430. Office Action at page 9.

For the reasons cited in the preceding subsection, Ricardo Martinez's declaration evidences Applicants' isolation and identification of the DNA and amino acid sequences of megakaryocyte tyrosine kinase 1 prior to Bennett *et al.* and Sakano *et al.* Accordingly, neither may be combined with the referenced Maniatis publication. Therefore, none of the claims are rendered obvious and, thus, this rejection is moot.

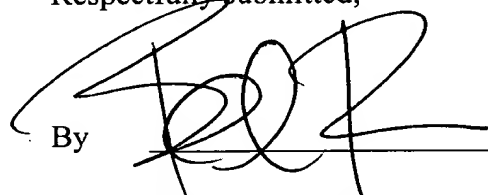
### III. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Date March 2, 2004

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5475  
Facsimile: (202) 672-5399

Respectfully submitted,

By   
Beth A. Burrous  
Attorney for Applicant  
Registration No. 35,087

PROJECT \_\_\_\_\_

Map Draw Indica of ORF

Page 1

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

Enzymes: All 335 enzymes (No Filter)

Settings: Linear, Certain Sites Only, Standard Genetic Code

GTGCAGCGGGACGCTCGGGTGTGCAGCCGGCTCGCGGAGGCCCTCTGGGGGGGGSGCSCGGGCGCGGCT  
CACGTCGCCCTGCGAGCCACACGTCGGCCGAGCGCTCCGGAGGACCCCCCCCCSCGSGCCCGCGCCGA

70

Only once

Below

SUG#301

SUG#313

V O R D A R V C S R L A E A S W G G ? ? G R G  
C S G T L G C A A G S R R P P G G G ? ? G A A  
C A A G R S G V O P A R G G L L G G G A R A R L

CGGGGGCGCCCCYTRAGCAGAAAACAGGRAGAACCAGGCTSGGTCHAGTGGCACCMAGCTCCCTACYTCY  
GCCCCGCGGGGRAYTCGTCTTTTGTCCYTCTTGGTCCGASCCAGKTCACCCTGGKTCGAGGGATGRAGR

140

Below

SUG#301

SUG#313

S G A P ? ? Q K T G R T R L G ? V A P S S L ? ?  
R G R P L S R K Q ? E P G ? V ? W H ? A P Y ?  
G G A P . A E N R ? N Q A ? S S G T ? L P T S

KGTGCMAGCCGCTKGCTGTGGCAGGCCAWTCCCARCGKYCCGACTGTGACCACTTGCTCAGTGTGCC  
MCACGKTCGGCGGAMCGGACACCGTCCGGTWAGGGTYGCMRGGGCTGACACTGGTGAACGAGTCACACGG

210

Below

SUG#301

SUG#313

V ? A A ? P V A G ? S Q R ? R L . P L A O C A  
? C ? P P ? L W Q A ? P ? ? P D C D H L L S V P  
? A S R L A C G R P ? P ? ? P T V T T C S V C

Read and Understood By

*R. M. H.*  
Signed

Date

*[Signature]*  
Signed

Date

0 0 1 2 9 6

PROJECT

## MKK1-3 consensus 4/12 Map (1 &gt; 2053) Site and Sequence

TCTCACSDGYCYCAKTTTCCCTCTGKGGGGCGATAGCGSGGCGAGGCTCTCTGGTTTCCTGGCGGGCAT 280  
 AGAGTGSHERGRGTNAAAGGGAGACCCCCGCTATCCGSCCGCTCCGAGAGACCAAAGGACCGCCCGTA

Below

SUG#301

SUG#313

SUG#304

SUG#304

S H ? ? ? F P S ? G R . A ? R G S L V S W R A  
 L T ? ? ? F P L ? G D R R G E A L W F P G G H  
 L S ? ? ? ? S L ? G A I G ? A R L S G F L A G I

TTCACGGCTGTGATTCTGCTGAGGAACCTCCCGGGTGAGCCCCCGCTTCTCCGAGCCTGGCACCCCCC 350  
 AAGTGCCGACACTAAGACGACTCCTTGAAGGGGCCACTCGGGGCGAAGGAGGCTCGGACCGTGGGGGG

One strand

SUG#313

SUG#313

SUG#304

SUG#304

F H G C D S A E E L P R V S P R F L R A W H P P  
 F T A V I L L R N F P G . A P A S S E P G T P  
 S R L . F C . G T S P G E P P L P P S L A P P

TCCCGTCTCAGCCAGGATGCCAACGAGGCGCTGGGCCCCGGGCACCCAGTGTATCACCAAATGCGAGCAC 420  
 AGGGCAGAGTCGGTCTACGGTTGCTCCGCGACCCGGGCCCCGTGGGTACATAGTGGTTTACGCTCGTG

One strand

SUG#313

SUG#313

SUG#304

SUG#304

SUG#301

P V S A R N P T R R W A P G T O C I T K C E H  
 L P S O P G C O R G A G P R A P S V S P N A S T  
 S R L S O D A N E A L G P G H P V Y H O M R A

light shaded residues show identical residues But in human  
 Gyl. (p.2)

RR Mr

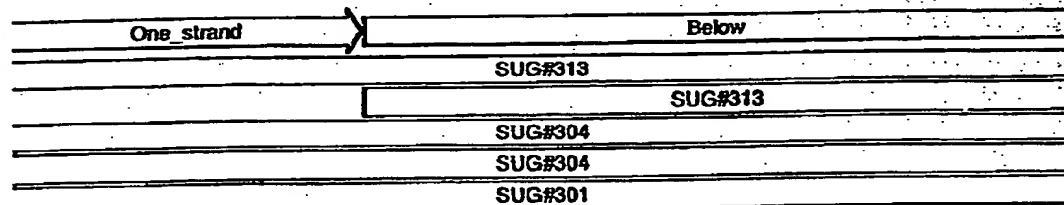
M. J. J.

PRO

Page 3

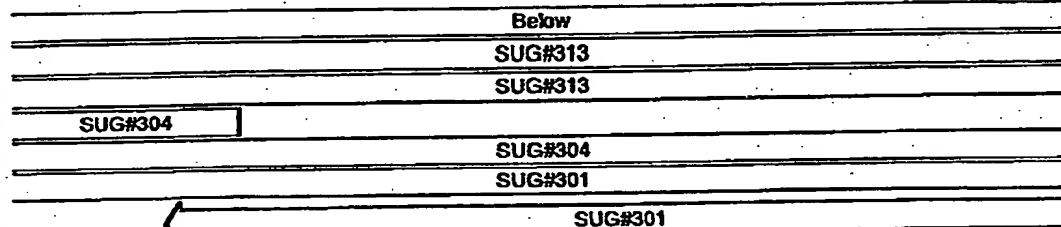
## MKK1-3 consensus 4/12 Map (1 &gt; 2053) Site and Sequence

ACCGCCCCAAGCCAGGGGAGCTGGCCTTCCGCAAGGGGCGACGTGGTCACCATCCTGGAGGCCTGCGAGA 490  
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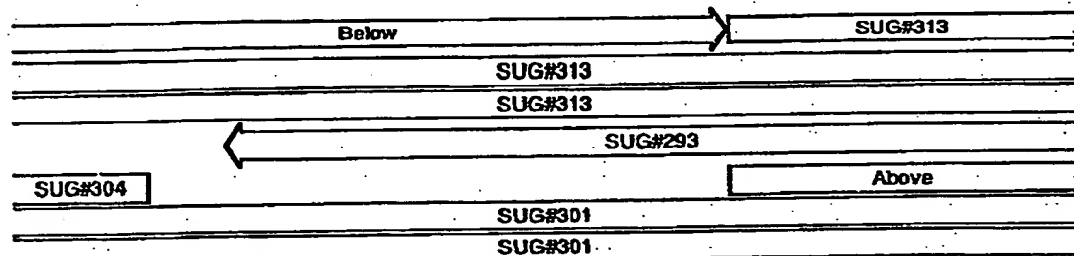
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 P A P S Q G S W P S A R A T W S P S W R P A R  
 H P P Q A R G A G L P Q G R R G H H P G G L R E

ACAAGAGCTGGTACCGCGTCAAGCACCAACAGTGGACAGGAGGGGCTGCTGGCAGCTGGGGCGCTGCG 560  
 TGTTCTCGACCATGGCGCAGTTCGTGGTGTGGTCACCTGTCTCCCGACGACCGTGGACCCCGGACGCG



N K S W Y R V K H H T S G O E G L L A A G A L R  
 T R A G T A S S T T P V D R R G C W O L G R C  
 Q E L V P R Q A P H O W T G G A A G S W G A

GGAGCGGGAGGCCCTCTCCGCAGACCCCAAGCTCAGCCTCATGCCGTGGTTCCACGGGAAGATCTCGGGC 630  
 CCTCGCCCTCCGGGAGAGGCGTCTGGGGTTCGAGTCGGAGTACGGCACCAAGGTGCCCTTCTAGAGCCCG



E R E A L S A D P K L S L H P W F H G K I S G  
 G S G R P S P O T P S S A S C R G S T G R S R A

Signed *[Signature]*

Date

Signature

*[Signature]*

Date

001297

## MKK1-3, consensus 4/12 Map (1 &gt; 2053) Site and Sequence

G G G P L R R P O A O P H A V V P R E D L G

CAGGAGGCTGTCCAGCAGCTGCAGCCTCCCGAGGATGGGCTGTTCTTGGTGGGGAGTCCGCGCGCCACC 700  
GTCCTCCGACAGGTCGTGACGTGGAGGGCTCTACCCGACAAGGACCACGCCCTCAGGCGCGCGGTGG

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#301

SUG#301

SUG#313

SUG#293

O E A V O O L O P P E D G L F L V R E S A R H  
R R L S S S C S L P R M G C S W C G S P R A T  
P G G C P A A A S R G W A V P G A G V R A P PCCGGCGACTACGTCTGTGCGTGAGCTTTGGCCGCGACGTATCCACTACCGCGTGCTGCACCGCGACGG 770  
GGCCGCTGATGCAGGACACGCACTCGAAACCGCGCTGCAGTAGGTGATGGCGCAGCAGCTGGCGCTGCC

SUG#313

SUG#313

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Above

SUG#301

SUG#313

SUG#293

P G D Y V L C V S F G R D V I H Y R V L H R D G  
P A T T S C A A L A A T S S T T A C C T A T  
R R L R P V R E L W P R R H P L P R A A P R R

KR M (Signed)

MHC

MR. S

MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

CCACCTCACAATCGATGAGGCCGTGTTCTTCTGCAACCTCATGGACATGGTGGAGCATTACAGCAAGGAC 840  
GGTGGAGTGTTAGCTACTCCGGCACAAGAAGACGTTGGAGTACCTGTACCACCTCGTAATGTCGTTCTCTG

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#313

SUG#313

SUG#293

H L T I D E A V F F C N L M D H V E H Y S K D  
A T S O S M R P C S S A T S W T W W S I T A R T  
P P H N R G R V L L O P H G H G G A L O O G

AAGGGCGCTATCTGCACCAAGCTGGTGAGACCAAAGCGGAAACACGGGACCAAGTCGGCCGAGGAGGAGC 910  
TTCCCGCGATAGACGTGGTTCGACCACTCTGGTTTCGCCCTTGTGCCCTGGTTCAGCCGGCTCCTCCTCG

SUG#313

SUG#313

SUG#313

SUG#293

Above

SUG#313

SUG#313

SUG#293

K G A I C T K L V R P K R K H G T K S A E E E  
R A L S A P S W D O S G N T G P S R P R R S  
O G R Y L H O A G E T K A E T R D O V G R G G A

TGGCCAGGGCGGGCTGGTTACTGAACCTGCAGCATTTGACATTGGGAGCACAGATCGGAGAGGGAGAGTT 980  
ACCGGTCCCGCCCGACCAATGACTTGGACGTCGTAACTGTAACCCTCGTGTCTAGCCTCTCCCTCTCAA

SUG#313

SUG#313

SUG#313

SUG#282

SUG#293

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SUG#313

SUG#282

SUG#313

R 52 [redacted]

[redacted]



MKK1-3 consensus 4/12 Map (1 &gt; 2053) Site and Sequence

SUG#293

L A R A G W L L N L O H L T L G A Q I G E G E F  
W P G R A G Y . T C S I . H W E H R S E R E S  
G O G G L V T E P A A F D I G S T D R R G R V

TGGAGYTGCCCTGCAGGGTGAGTACCTGGGGCAAAGGTGGCCGTGAAGAATATCAAGTGTGATGKACA  
ACCTCRACRGGACGTCCCACCTCATGGACCCCGTTTCCACCGGCAGTTCCTTATAGTTCACACTACANTGT

1050

SUG#313

SUG#313

SUG#282

SUG#293

Above

SUG#313

SUG#282

SUG#313

SUG#293

SUG#301

(Purified not pure)  
G ? ? L O G E Y L G O K V A V K N I K C D V T  
L E L ? C R V S T W G K R W P . R I S S V H ? O  
W S C P A G . V P G A K G G R E E Y O V . C ?

GCCCAGGCCTTCCTGGACGAGACGGCCGTCATGACGAAGATGCAACACGAGAACCTGGTGCGTCTCCTGG  
CGGGTCCGGAAGGACCTGCTCTGCCGGCAGTACTGCTTCTACGTTGTGCTCTTGGACCACGCAGAGGACC

1120

SUG#313

SUG#313

SUG#282

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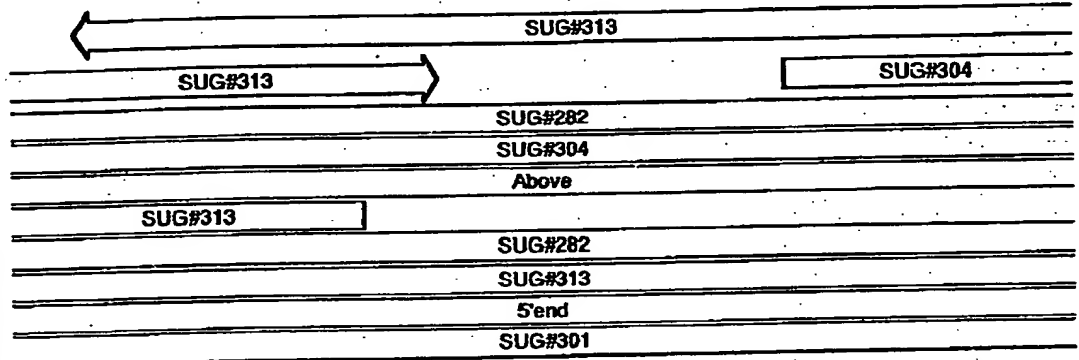
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S P G L P G R D G R H D E D A T R E P G A S P G

U R M R

M R

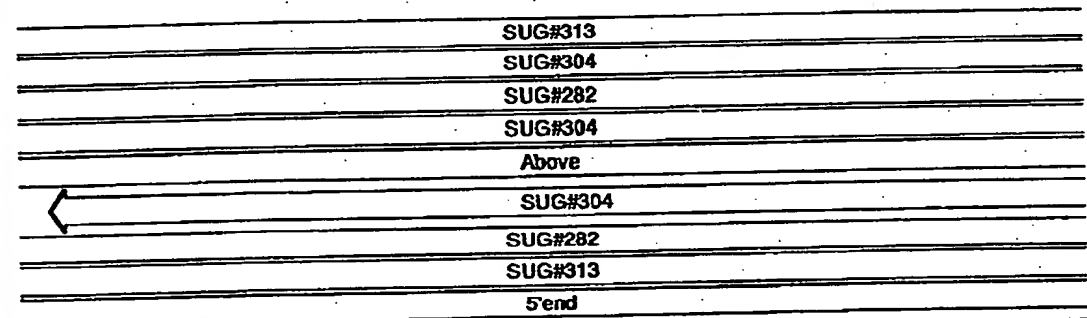
██████████  
MKK1-3 consensus 4/12 Map (1 > 2053) Site and Sequence

GCCTGATCCTGCACCAGGGGCTGTACATTGTCATGGAGCACGTGAGCAAGGGCAACCTGGTGAACCTTTCT 1190  
CGCACTAGGACGTGGTCCCCGACATGTAACAGTACCTCGTGCACCTCGTTCCCGTTGGACCACTTGAAAGA



G V I L H O G L Y I V M E H V S K G N L V N F L  
A S C T R G C T L S W S T A R A T W T F  
R D P A P G A V H C H G A R E Q G O P G E L S

BCGGACCCGGGGTCGAGCCCTCGTGAACACCGCTCAGCTCCTGCAGTTTTCTCTGCACGTGGCCGAGGGC 1260  
CGCCTGGGCCCCAGCTCGGGAGCACTTGTGGCGAGTCGAGGACGTCAAAGAGACGTGCACCGGCTCCCG



R T R G R A L V N T A Q L L O F S L H V A E G  
C G P G V E P S T P L S S C S F L C T W P R A  
A D P G S S P R E H R S A P A V F S A R G R G

RZ Mtn  
Signed

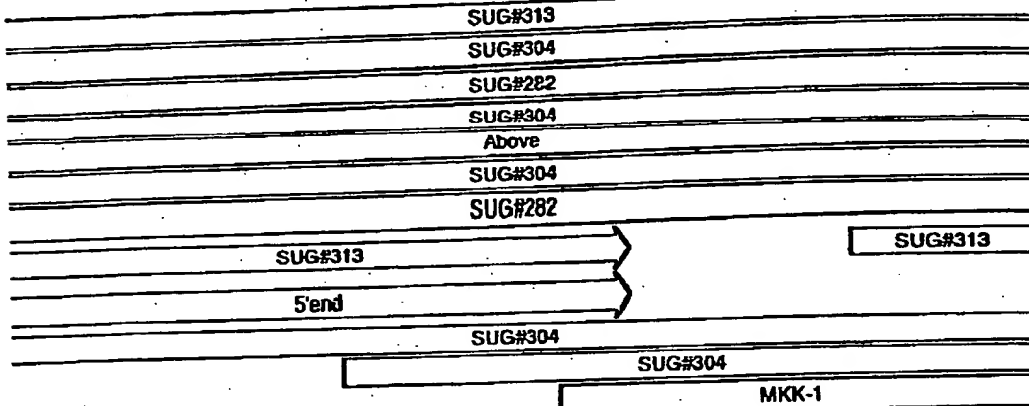
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Date

mfart  
Signed

██████████  
Date

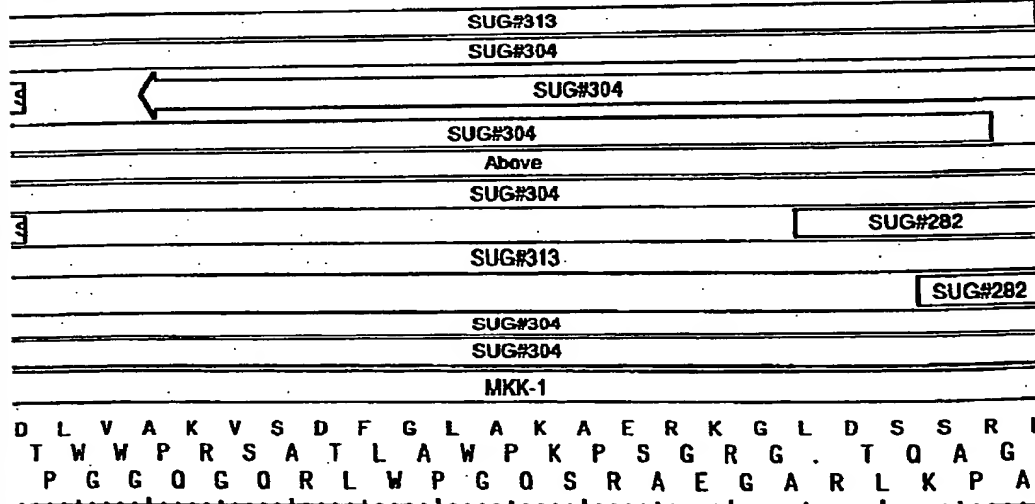
MKK1-3 consensus 4/12 Map (1 &gt; 2053) Site and Sequence

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TACCTCATGCACTCTCGTTCTTCTGAACACGTGGCGCTGGACCGGCGGCGTGTAGGACCAGAGTCTCC



H E Y L E S K K L V H R D L A A R N I L V S E  
W S T W R A R S L C T A T W P P A T S W S O R  
H G V P G E O E A C A P R P G R P O H P G L R G

ACCTGGTGGCCAAGGTCAGCGACTTTGGCCTGGCCAAAGCCGAGCGGAAGGGGCTAGACTCAAGCCGGCT 1400  
TGGACCACCGGTTCCAGTCGCTGAAACCGGACCGGTTTCGGCTCGCCTTCCCCGATCTGAGTTCGGCCGA



*R. R. M.*  
Signed

Date

*M. R. M.*  
Signed

Date

## MKK1-3 consensus 4/12 Map (1 &gt; 2053) Site and Sequence

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G C C C G T C A A G T G G A C G G C G C C G A G G C T C T C A A A C A C G G G A A G T T C A C C A G C A A G T C G G A T G T C T G G A G T  
-----  
C G G G C A G T T C A C C T G C C G C G G G C T C C G A G A G T T T G T G C C C T T C A A G T G G T C G T T C A G C C T A C A G A C C T C A  
-----

1470

Below

SUG#304

SUG#304

Above

SUG#304

SUG#282

SUG#313

SUG#282

SUG#304

SUG#304

MKK-1

P V K W T A P E A L K H G K F T S K S D V W S  
C P S S G R R P R L S N T G S S P A S R M S G V  
A R Q V D G A R G S Q T R E V H Q Q V G C L E  
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T T T G G G G T G C T G C T C T G G G A G G T C T T C T C A T A T G G A C G G G C T C C G T A C C C T A A A A T G T C A C T G A A A G A G G  
-----  
A A A C C C C A C G A C G A G A C C C T C C A G A A G A G T A T A C C T G C C C G A G G C A T G G G A T T T T A C A G T G A C T T T C T C C  
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1540

Below

SUG#304

SUG#304

SUG#282

SUG#313

SUG#282

SUG#304

F G V L L W E V F S Y G R A P Y P K M S L K E  
L G C C S G R S S H M D G L R T L K C H K R  
F W G A A L G G L L I W T G S V P N V T E R G  
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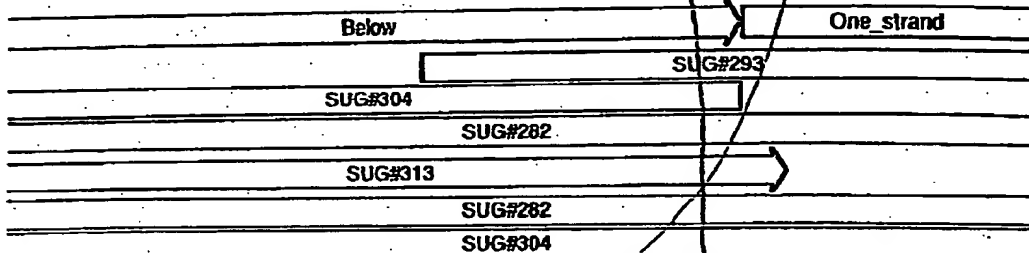
RR hr  
signed

mf  
signed

Possible ORF change  
Terminator to start (from)  
3000 later (see P. 23)

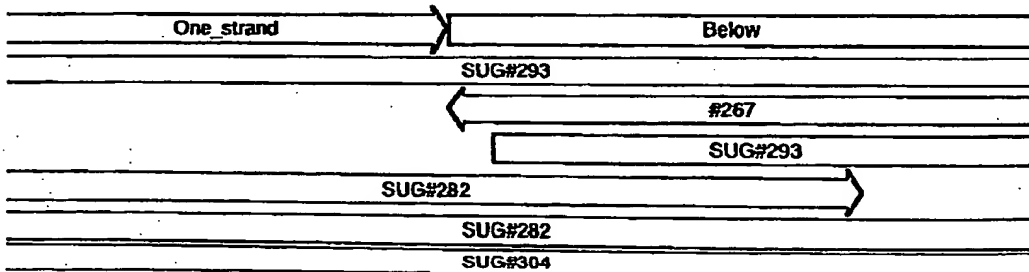
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ACAGCCTCCGGGACCTCTTCCCCATGGCGTACCTTGGGGGGGCTCCACAGGTCCGGGCACGTGCATGA



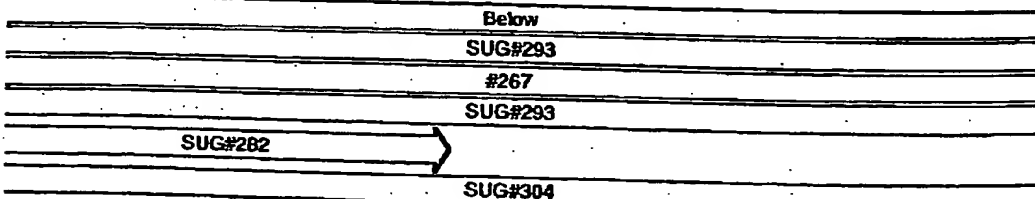
V S E A L E K G Y R H E P P R G S R P V H V L  
C R R P W R R G T A W N P P E G C P G P C T Y  
V G G P G E G V P H G T P P R A V O A R A R T

CATGAGCAGCTGCTGGGAGGCAGAGCCCGCCGCCGCCACCCTTCCGCAAACTGGCCGAGAAGCTGGCCCC 1680  
GTACTCGTCGACGACCCCTCCGTCTCGGGGGGGGCCGGTGGGAAGGCGTTTGACCGGCTCTTCGACCGGG



H S S C W E A E P A A G H P S A N W P R S W P  
S C A A A G R O S P P P A T L P O T G R E A G P  
H E O L L G G R A R R R P P F R K L A E K L A

GGGAGCTACGCAGTGCAGGTGCCCCAGCCTCCGTTCTCAGGGCAGGACGCCGAGGCTCCACCTCGCCCC 1750  
CCCTCGATGCGTCACGTCCACGGGGTGGAGGCAAGAGTCCCGTCTGCGGCTGCCGAGGTGGAGCGGGG



G S Y A V O V P Q P P F S G O D A D G S T S P  
G A T O C R C P S L R S O G R T P T A P P R P

Rem

MR

## MKK1-3 consensus 4/12 Map (1 &gt; 2053) Site and Sequence

R E L R S A G A P A S V L R A G R R R L H L A P

GAAGCCAGGAGCCCTGACCCCAACCGGTGGGGCCCTTGGCCAGAGGACCGAGAGAGTGGAGAGTACGGC  
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1820

Below

SUG#293

#267

SUG#293

SUG#304

R S O E P P H P V G P L A O R T E R V E S T A  
E A R S P D P T R W G P W P R G P R E W R V R  
K P G A L T P P G G A L G P E D R E S G E Y G

GTGGGGGCACTGACCAGGCCCAAGGAGGGTCCAGGCGGGCAAGTCATCCTCCTGGTGGCCACAGCAGGGG  
CACCCCGTGACTGGTCCGGGTCTCTCCAGGTCCGCCGTTAGTAGGAGGACCACGGGTGTCGTCCCC

1890

Below

SUG#293

#267

SUG#293

W G H P G P R R V O A G K S S S W C P O O G  
R G G T D O A O G G S R R A S H P P G A H S R G  
V G A L T R P K E G P G G O V I L L V P T A G

CTGGCCACGTAGGGGGCTCTGGGCGGCCCGTGGACACCCAGACCTGCGAAGGATGATCGCCCGATAAA  
GACCGGSGCATCCCCGAGACCCGCCGGGCACCTGTGGGGTCTGGACGCTTCTACTAGCGGGCTATT

1960

Below

SUG#293

#267

SUG#293

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A G P R R G L W A A R G H P R P A K D D R P I K

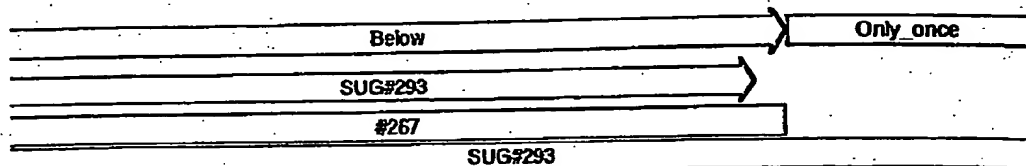
Rz Mr  
Signed

Mr  
Signed

001301

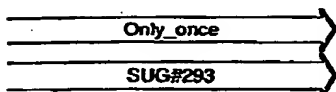
## MKK1-3 consensus 4/12 Map (1 - 2053) Site and Sequence

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R R I L R T L K K G G A R Y P I R P I V S R I K  
 D G F . G L . K K G G P G T O F A L . V V L  
 T D S K D S K K R G G P V P N S P Y S E S Y

AATTAAC TGGCCGTCGTTTAA T 2053  
 TTAATTGACCGGCAGCAAATTA



I N W P S F  
 K L T G R R F N  
 N . L A V V L M

PR [redacted]

mf [redacted]